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09/651,181	08/30/2000	Todd A. Dickinson	A-68392-2/DJB/RMS/DCF	2424

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FLEHR HOHBACH TEST ALBRITTON & HERBERT LLP
Suite 3400
Four Embarcadero Center
San Francisco, CA 94111-4187

EXAMINER	
CHAKRABARTI, ARUN K.	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/651,181	Dickinson
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- ***The MAILING DATE of this communication appears on the cover sheet with the correspondence address*** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 7, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-10, 17-24, 29-31, and 47* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-10, 17-24, 29-31, and 47* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claim 17 has been amended and new claim 47 has been added. Claims 1-10, 17-24, and 29-31 and 47 are pending in this application.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 1-8, 10, and 29-31 are rejected under 35 U.S.C. 102(a) as being anticipated by Barker et al. (Analytical Chemistry, (1998), Vol. 70, pages 4902-4906).

Barker et al teach a composition comprising:

a) a substrate with a surface comprising discrete sites;

b) a reflective coating on the surface; and

c) a population of microspheres distributed on the substrate, the microspheres comprising at least a first and a second subpopulation (Abstract and Experimental Section, Sensor Preparation and Optical Apparatus for fluorescence and absorbance spectroscopies subsection).

Barker et al teach a composition wherein at least one subpopulation comprises a bioactive agent (Figure 6 and Table 2).

Barker et al teach a composition, wherein the substrate comprises a first and a second surface, wherein the first surface comprises the discrete sites, the reflective coating on the second surface, the population of microspheres distributed on the first surface (Abstract and Experimental Section, Sensor Preparation Subsection).

Barker et al teach a composition, wherein the substrate is a fiber optic bundle (Abstract and Experimental Section, Sensor Preparation and Optical Apparatus for fluorescence and absorbance spectroscopies subsection).

Barker et al teach a composition, wherein the fiber optic bundle comprises wells comprising the microspheres (Abstract and Experimental Section, Sensor Preparation and Optical Apparatus for fluorescence and absorbance spectroscopies subsection).

Barker et al teach a composition, wherein the substrate is selected from plastic (Sensor Preparation Subsection).

Barker et al teach a composition, wherein the reflective coating is a metal (Abstract and Sensor Preparation Subsection under Experimental Section).

Barker et al teach a composition, wherein the metal is gold (Abstract and Sensor Preparation Subsection under Experimental Section).

Barker et al teach a composition, wherein the reflective coating selectively absorbs certain wavelengths (Abstract and Sensor Preparation Subsection under Experimental Section and Figures 1-4).

Barker et al teach an array composition comprising:

a) a substrate with a surface comprising discrete sites (Abstract and Sensor Preparation Subsection under Experimental Section);

b) a population of microspheres distributed on the substrate, wherein the microsphere comprise:

I) a bioactive agent; and

ii) a signal transducer element which is a nucleotide intercalator as well as a fluorophore (Abstract and Experimental Section, Sensor Preparation Subsection and optical apparatus for fluorescence and absorbance spectroscopies subsection).

4. (e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

5. Claim 47 is rejected under 35 U.S.C. 102(b) as being anticipated by Kedar et al. (U.S. Patent 6,198,577 B1) (March 6, 2001).

Kedar et al. teaches an array composition comprising a substrate with a surface comprising discrete sites comprising alternatively shaped wells, wherein the wells have a cross section selected from the group consisting of a square, a star, a triangle, a pentagon and an octagon (Figure 12 and Column 11, lines 1-28).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 17-20 and 22-23 are rejected under 35 U.S.C. 103(a) over Barker et al. (Analytical Chemistry, (1998), Vol. 70, pages 4902-4906) in view of Walt et al. (U.S. Patent 6,023,540) (February 8, 2000).

Barker et al. teach a composition of claims 1-8, 10, and 29-31 and also the composition, wherein the substrate is a transparent substrate comprising a first and a second surface, the first surface comprising discrete sites, and a reflective coating on the second surface (Abstract and Experimental Section, Sensor Preparation and Optical Apparatus for fluorescence and absorbance spectroscopies subsection).

Barker et al do not teach a composition comprising a substrate with a surface comprising discrete sites comprising alternatively shaped wells.

Walt et al teach an array composition comprising a substrate with a surface comprising discrete sites comprising alternatively shaped wells (Figures 5A-5B and 7A-7B and Claim 57).

Barker et al do not teach a composition, wherein the wall angle is of the alternatively shaped wells is a sloped wall angle.

Walt et al teach an array composition, wherein the wall angle is of the alternatively shaped wells is a sloped wall angle (Figures 5A-5B and 7A-7B).

Barker et al do not teach a composition,wherein the alternatively shaped wells contain a rounded wall interior.

Walt et al teach an array composition,wherein the alternatively shaped wells contain a rounded wall interior (Figures 5A-5B and 7A-7B).

Barker et al do not teach an array composition, wherein at least one of the alternatively shaped wells is a geometrically shaped well having a cross section selected from a square, a hexagon, a star, a triangle, a pentagon, and a octagon.

Walt et al teach an array composition, wherein at least one of the alternatively shaped wells is a geometrically shaped well having a cross section selected from a square, a hexagon, a star, a triangle, a pentagon, and a octagon (Figures 5A-5B and 7A-7B).

Barker et al do not teach an array composition, further comprising a population of microspheres distributed in the wells

Walt et al teach an array composition, further comprising a population of microspheres distributed in the wells (Figure 6).

Walt et al further teach an array composition, wherein the population comprises at least first and second subpopulation, each of the subpopulations comprising a bioactive agent (Column 4, lines 10-14 and Column 8, line 65 to Column 11, line 25 and Claim 39).

It would have been further *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a composition, wherein the substrate is a transparent substrate comprising a first and a second surface, the first surface comprising discrete sites, and a reflective coating on the second surface of Barker et al. into the composition of Walt et al, since Barker et al. state, "The new fluorescein derivative chemical sensors have characteristics similar to those of the protein-based biosensors, including fast response times, excellent selectivity, and complete reversibility. In addition, the chemical sensors have advantages such as greater stability and commercially available components (Abstract, lines 12-17). " Moreover, Walt et al provides further motivation as Walt et al state, "Moreover, since the beads and fibers in the array can be monodisperse, the fluorescent regions arising from signal generation are extremely uniform and can be analyzed automatically using commercially available microscopy analysis software, such image processing software is capable of defining different special regions automatically and counting the number of segments within each region in several seconds (Column 4, lines 20-27)". By employing scientific reasoning, an ordinary artisan would have combined and substituted a composition, wherein the substrate is a transparent substrate comprising a first and a second surface, the first surface comprising discrete sites, and a reflective

coating on the second surface of Barker et al. into the composition of Walt et al, in order to improve the synthesis of array of biomolecules. An ordinary practitioner would have been motivated to combine and substitute a composition, wherein the substrate is a transparent substrate comprising a first and a second surface, the first surface comprising discrete sites, and a reflective coating on the second surface of Barker et al. into the composition of Walt et al, in order to achieve the express advantages , as noted by Barker et al., of an invention which provides greater stability and commercially available components in addition to fast response times, excellent selectivity, and complete reversibility and also to achieve the express advantages , as noted by Walt et al., of an invention which provides image processing software capable of defining different special regions automatically and counting the number of segments within each region in several seconds.

8. Claim 9 is rejected under 35 U.S.C. 103(a) over Barker et al. (Analytical Chemistry, (1998), Vol. 70, pages 4902-4906) in view of Toriumi et al. (U.S. Patent 5,896,227) (April 20, 1999).

Barker et al teach a composition of claims 1-8, 10, and 29-31 as described above.

Barker et al do not teach a composition, wherein the reflective coating is a dielectric coating.

Toriumi et al teach a composition, wherein the reflective coating is a dielectric coating (Column 7, lines 42-45 and lines 50-52).

It would have been further *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a composition, wherein the reflective

coating is a dielectric coating of Toriumi et al. into the method of Barker et al, since Toriumi et al. state, "Preferably the microspheres have a reflective coating on a portion thereof, e.g., a hemispheric coating of aluminum, silver or a dielectric coating. Such microspheres will be self-retroflecting (Column 7, lines 42-45). ". By employing scientific reasoning, an ordinary artisan would have combined and substituted a composition, wherein the reflective coating is a dielectric coating of Toriumi et al. into the method of Barker et al, in order to improve the synthesis of array of biomolecules. An ordinary practitioner would have been motivated to combine and substitute a composition, wherein the reflective coating is a dielectric coating of Toriumi et al. into the method of Barker et al in order to achieve the express advantages , as noted by Toriumi et al., of an invention which provides microspheres which are self-retroflecting.

9. Claim 21 is rejected under 35 U.S.C. 103(a) over Barker et al. (Analytical Chemistry, (1998), Vol. 70, pages 4902-4906) in view of Walt et al. (U.S. Patent 6,023,540) (February 8, 2000) further in view of Kedar et al. (U.S. Patent 6,198,577 B1) (March 6, 2001).

Barker et al. in view of Walt et al teach the composition of claims 17-20, and 22-23 as described above.

Barker et al. in view of Walt et al. do not teach a composition, wherein the geometrically shaped well has a cross section selected from the group consisting of a square, a hexagon, a star, a triangle, a pentagon and an octagon.

Kedaret al teach a composition, wherein the geometrically shaped well has a cross section selected from the group consisting of a square, a hexagon, a star, a triangle, a pentagon and an octagon.

It would have been further *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a composition, wherein the geometrically shaped well has a cross section selected from the group consisting of a square, a hexagon, a star, a triangle, a pentagon and an octagon of Kedar et al. into the method of Barker et al. in view of Walt et al, since Kedar et al. state, "Setting the magnification so that each square well in the multiwell plate is imaged onto an integer number of pixels in the imaging device as described above is advantageous in part because it aids in minimizing cross-talk between adjacent wells, and simplifies subsequent digital analysis of the image (Column11, lines 13-18). " By employing scientific reasoning, an ordinary artisan would have combined and substituted a composition, wherein the geometrically shaped well has a cross section selected from the group consisting of a square, a hexagon, a star, a triangle, a pentagon and an octagon of Kedar et al. into the method of Barker et al. in view of Walt et al in order to improve the synthesis of array of biomolecules. An ordinary practitioner would have been motivated to combine and substitute a composition, wherein the geometrically shaped well has a cross section selected from the group consisting of a square, a hexagon, a star, a triangle, a pentagon and an octagon of Kedar et al. into the method of Barker et al. in view of Walt et al in order to achieve the express advantages , as noted by Kedar et al., of an invention which is advantageous in part because it aids in minimizing cross-talk between adjacent wells, and simplifies subsequent digital analysis of the image.

10. Claim 24 is rejected under 35 U.S.C. 103(a) over Barker et al. (Analytical Chemistry, (1998), Vol. 70, pages 4902-4906) in view of Walt et al. (U.S. Patent 6,023,540) (February 8, 2000) further in view of Toriumi et al. (U.S. Patent 5,896,227) (April 20, 1999).

Barker et al. in view of Walt et al teach the composition of claims 17-20, and 22-23 as described above.

Barker et al. in view of Walt et al. do not teach a composition with a reflective coating on the second surface.

Toriumi et al teach a composition with a reflective coating on the second surface (Column 7, lines 42-45 and lines 50-52).

It would have been further *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a composition, wherein the reflective coating is a metal or dielectric coating of Toriumi et al. into the method of Barker et al. in view of Walt et al, since Toriumi et al. state, "Preferably the microspheres have a reflective coating on a portion thereof, e.g., a hemispheric coating of aluminum, silver or a dielectric coating. Such microspheres will be self-retroflecting (Column 7, lines 42-45). " Moreover Walt et al state, "A microsphere-based analytic chemistry system is disclosed in which microspheres carrying different chemical functionalities may be mixed together while the ability is retained to identify the functionality on each bead using an optically interrogatable encoding scheme (Abstract, first sentence)". By employing scientific reasoning, an ordinary artisan would have combined and substituted a composition, wherein the reflective coating is a dielectric coating of Toriumi et al. into the method of Walt et al, in order to improve the synthesis of array of biomolecules. An ordinary practitioner would have been motivated to combine and substitute a composition, wherein the reflective coating is a dielectric coating of Toriumi et al. into the method of Barker et al. in view of Walt et al in order to achieve the express advantages , as noted by Toriumi et

al., of an invention which provides microspheres which are self-retroflecting and also to achieve the express advantages, as noted by Walt et al., of a system which provides a microsphere-based analytic chemistry system in which microspheres carrying different chemical functionalities may be mixed together while the ability is retained to identify the functionality on each bead using an optically interrogatable encoding scheme.

Response to Amendment

11. In response to amendment, previous 102 (e) rejection in view of Walt et al has been withdrawn. However, a new 102 (e) and 103 (a) rejections have been included.

Response to Arguments

12. Applicant's arguments filed on February 7, 2003 have been fully considered but they are not persuasive.

Applicant argues that 102(a) rejection as anticipated by Barker et al is improper and should be withdrawn. Applicant argues that Barker does not teach the first and second subpopulation of microspheres. This argument is not persuasive. Barker clearly teaches reference microspheres deposited on the sensor as mentioned in the rejection. Reference microspheres can be considered as a combination of first and second subpopulation of microspheres, because it is not a requirement of the claim that the first and second subpopulation of microspheres have to be different.

Moreover, applicant argues that the bioactive agent of the sensor, as taught by Barker, is not on the microspheres, rather it is attached to the gold that is assembled on the substrate. This argument is not persuasive, especially in the presence of "comprising" language of the claim, any additional material(s) or step(s) can be added in the claim. Therefore, Barker clearly anticipates the claims 1-8, 10, and 29-31 and accordingly, 102(a) rejection based on Barker is hereby properly maintained.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Barker et al since Barker et al. state, "The new fluorescein derivative chemical sensors have characteristics similar to those of the protein-based biosensors, including fast response times, excellent selectivity, and complete reversibility. In addition, the chemical sensors have advantages such as greater stability and commercially available components (Abstract, lines 12-17). " The same logic is applicable to other references as well.

Applicant then argues the 103 rejections are improper because it lacks a reasonable expectation of success.

With regard to the " lacks a reasonable expectation of success" argument, The MPEP 2143.02 states

"Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart , 531 F.2d 1048, 189 USPQ 143 (CCPA 1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also Amgen, Inc. v. Chugai Pharmaceutical Co ., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied , 502 U.S. 856 (1991) (In the context of a biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); In re O'Farrell , 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.)."

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Barker reference of the enabling methodology, the suggestion to modify the prior art, and evidence that a number of different array compositions with a) a substrate with a surface comprising discrete sites;

b) a population of microspheres distributed on the substrate,

I) a bioactive agent; and

ii) a signal transducer element which is a nucleotide intercalator as well as a fluorophore, were actually experimentally studied and found to be functional (Abstract and Sensor Preparation Subsection under Experimental Section and optical apparatus for fluorescence and absorbance spectroscopies subsection). This evidence of functionality trumps the attorney arguments, which argues that Barker reference is an invitation to research, since Barker steps beyond research and shows the functional product.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti
Patent Examiner
Art Unit 1634
March 18, 2003

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600